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| EXAMINER | |
|---|---|
| PURDY, KYLE A | |

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| 1611 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/561,700 | ODIDI ET AL. | |
| | Examiner | Art Unit | |
| | Kyle Purdy | 1611 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *2/3/2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *29,30 and 46-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28 and 31-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3 pages (2/12/2010 and 04/29/2010)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of Application*

1. The Examiner acknowledges receipt of the amendments filed on 02/03/2010 wherein claims 1 and 31 have been amended.

2. Claims 1-28 and 31-45 are presented for examination on the merits. The following rejections are made.

### *Response to Applicants' Arguments*

3. Applicants arguments filed 02/03/2010 regarding the objection to the specification have been fully considered and are found responsive. The objection has been overcome in view of the amendment to the specification.

4. Applicants arguments filed 02/03/2010 regarding the rejection of claims 1-28 and 31-45 made by the Examiner under 35 USC 103(a) over Phillips (US 2002/0045646) in view of Bergstrand et al. (US 5817338) and Chen (US 2001/0006649) have been fully considered but they are not found persuasive.

5. The rejection of claims 1-28 and 31-45 made by the examiner under 35 USC 103(a) is **MAINTAINED** for the reasons of record in the office action mailed on 09/03/2009.

6. In regards to the 103(a) rejection, Applicant asserts the following:

**A)** The claims as amended overcome the previous rejection by describing the composition as one that comprises three separate and distinct populations.

7. In response to A, the claims as amended do not recite that which Applicant suggests. The claims require a composition comprising "multiple populations of at least one of beads, pellets,

tablets and granules provided in a capsule". The components of Applicants claimed capsules are distinct in that they are their own separate entities with distinct functions, functions different from the other components also contained within the capsule. This amendment does not distinguish the claim from the prior art. Applicant is directed to [0015] of Phillips which states that proton pump inhibitors such as omeprazole can be formulated into a "powder mixture" which is then formulated into "enteric-coated small beads, pellets, tablets and may be loaded into capsules". Thus, taking Phillip's overall invention in view of this suggestion, one would have readily envisioned preparing a capsule comprising i) a population of base (i.e. sodium bicarbonate); ii) a population of pharmaceutical substance (i.e. a PPI); iii) a population of enteric coated pharmaceutical substance; and iv) a population of enteric coated basic substance wherein these substances are each provided as a powder, bead or granule and filled into a capsule. Such an undertaking would have been obvious because choosing from a finite number of identified, predictable solutions/formulations with a reasonable expectation for success [in treating gastric disorders] is *prima facie* obvious. Applicants arguments are not persuasive.

## Maintained Rejections, of Record
### *Claim Rejections - 35 USC § 103*

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. **Claims 1-28 and 31-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips (US 2002/0045646; of record) in view of Bergstrand et al. (US 5817338, 10/06/1998; of record) and Chen (US 2001/0006649; published 07/05/2001).**

11. Phillips is drawn to a composition for treating gastric disorders employing proton pump inhibitors (PPIs) in a pharmaceutically acceptable carrier. It is taught that the PPI can be any substituted benimidazole compound possessing $H^+$, $K^+$-ATPase inhibiting activity and being unstable to acid (i.e. acid labile). The composition of Phillips can be a powder, tablet, capsule and a two part tablet (see [0036]; see instant claims 1 and 31). It is taught that upon oral administration of the PPI the drug may be absorbed into the bloodstream where the compound is eventually delivered to the acid secreting portion of the parietal cells of the stomach. The PPIs included within the teaching of Phillips include omeprazole, lansoprazole and rabeproazole. It is noted by Phillips that such PPIs are readily degraded under acidic conditions such as that of the stomach and a useful way to circumvent degradation is to include at least one buffering agent (i.e. basic substance). Basic substance include sodium bicarbonate, magnesium hydroxide and aluminum hydroxide (see [0054]; see instant claims 21 and 40). Moreover, the basicity of base used must be strong enough to elevate the pH of the stomach sufficiently to prevent significant

degradation of the drug and to achieve ample bioavailability of the drug to induce a therapeutic effect.

12. Example VI teaches a multi-functional tablet comprising two discrete drug delivery systems i) free omeprazole and free sodium bicarbonate (rapid release) and ii) enterically coated omeprazole granules (slow release) (see [0176]; see instant claims 1-6, 10, 13, 18-21, 31). The tablet is taught to contain known binders and excipients (see [0176]; see instant claims 7 and 8). Such excipients include disintegrant such as cross-linked sodium carboxymethylcellulose (sodium croscarmellose) and fillers such as calcium lactate (see Example 1, B1 at page 10; see instant claims 8 and 28). The tablets of Example VI were formulated to deliver a bolus and a time-released dose of the PPI omeprazole (i.e. pulsed release, see instant claim 6). Upon ingestion of the tablet, the tablet dissolves, freeing the non-enteric coated base and omperazole into the stomach (see [0176], see instant claim 22). The basic substance increases the pH of the stomach, preventing the omeprazole from acidic degradation, and allows omeprazole to be absorbed by the parental cells of the stomach. Meanwhile, the enterically coated omeprazole is absorbed in the duodenum (see [0176]; see instant claim 23, 44 and 45). It's noteworthy that four-hours post administration, the pH of the stomach is raised to an average of 7.1 (see Figure 3, see instant claim 24).

13. Although the teaching of Phillips motivates one to include an enterically coated omeprazole granule with free base and omeprazole, it still fails to teach the components of the enterically coated granule. Phillips teaches the base and omeprazole as being in the form of a powder, rather than a granule.

14. The teaching of Bergstrand is drawn to a pharmaceutical tablet dosage form containing omeprazole. The table of Bergstrand comprises a core substance which contains an acid susceptible substance such as omeprazole, followed by a first coating (separating layer), and then a second coating (an enteric coating) (see column 5, line 60 - column 6, line 35; see instant claims 13-17, 32+33). The separating layer includes alkaline gents to enhance the pH-buffering properties. This necessarily improves the stability of the acid labile omeprazole contained within the core as it prevents degradation of the drug during long periods of storage. Alkaline agents include compounds typically used in antacid formulations such as calcium hydroxide, sodium phosphate, and so on (see column 6, lines 20-30). The omeprazole granule of Bergstrand may be mixed with basic substances such as those discussed above (calcium hydroxide, etc.; see column 6, lines 20-30). The materials used for the enteric coating includes polyethylene glycol and polyvinyl acetate (see column 6, lines 45-55; see instant claim 27). As an example an omeprazole granule is found at Example 10.

15. Chen is directed to stable oral pharmaceutical formulations comprising omeprazole. It is taught that omeprazole and an alkaline inorganic substance may be a powder or a granule (see [0040]).

16. Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to combine the teachings of Phillips, Bergstrand and Chen because in doing so would result in a composition which possess a population comprising:

i) a population of base (i.e. sodium bicarbonate);

ii) a population of pharmaceutical substance (i.e. a PPI);

iii) a population of enteric coated pharmaceutical substance; and

iv) a population of enteric coated basic substance.

The significance of Phillips is that it teaches a multi-functional tablet compositions comprising

i) a population of base (i.e. sodium bicarbonate);

ii) a population of pharmaceutical substance (i.e. a PPI);

iii) a population of enteric coated pharmaceutical substance; and

The multifunctional tablet is manufactured to possess rapid and delayed-release functionalities (pulse release) wherein the pharmaceutical substance is present in both functionalities and the basic substance is present in the rapid release portion. It's noted that the example relied upon in Phillips is directed to a tablet, rather than a capsule. However, it would have been obvious to any person of ordinary skill to take the formulation of Example VI, and fill it into a capsule rather than compressing into a tablet. Such a composition is suggested by the reference, and one would have had a reasonable expectation in arriving at a pulsed-release composition with the instantly claimed properties. Additionally, it is noted that Phillips teaches using powders in Example VI. However, the prior art illustrates that powders and granules are obvious variants and thus, one is obvious is over other the other and the substitution of one for the other would result in a product capable of pulsed release of the omeprazole. Although the teaching of Phillips includes an enterically coated PPI population, it fails to teach an enterically coated granule with a separating layer. One of ordinary skill would be motivated to look to the art to see how to make an enterically coated PPI granule capable of effectively delivering the active substance to the body.

17. Bergstrand teaches PPI containing granules coated with a first separating layer followed by a second enteric polymer coating, wherein the enteric granule contains antacids such as sodium bicarbonate. Thus, one of ordinary skill would be motivated to include the granule of

Bergstrand with the teaching of Phillips to arrive at an invention with the instantly claimed properties (see i-iv above). With respect to the recited properties such as rapid release of the rapidly released basic substance increasing the pH of the stomach to more than 4 and less than about 7 in less than 1 hour carries no patentable weight. Such a property would be obvious to optimize, as noted above, the stability of the PPIs as well as their pharmaceutical efficacy is dependent upon the pH of their local environment. If the pH of the stomach isn't rapidly alkalinized, the drug will not be effective. Moreover, as both references are within the same general field of endeavor (delivery of antacids and PPIs), it follows that combination would be obvious and would result in a therapeutic composition having the properties of the instantly claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### *Conclusion*

18. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

19. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

21. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau, can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

22. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*/Kyle Purdy/*
*Examiner, Art Unit 1611*
*July 28, 2010*

/Sharmila Gollamudi Landau/
Supervisory Patent Examiner, Art Unit 1611